Complete Summary

GUIDELINE TITLE

Improving the diagnosis and treatment of smear-negative pulmonary and extrapulmonary tuberculosis among adults and adolescents. Recommendations for HIV-prevalent and resource-constrained settings.

BIBLIOGRAPHIC SOURCE(S)

World Health Organization (WHO). Improving the diagnosis and treatment of smear-negative pulmonary and extrapulmonary tuberculosis among adults and adolescents. Recommendations for HIV-prevalent and resource-constrained settings. Geneva: Switzerland: World Health Organization (WHO); 2007. 36 p. [33 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Smear-negative pulmonary and extrapulmonary tuberculosis
- Human immunodeficiency virus (HIV) infection

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Pediatrics
Preventive Medicine
Pulmonary Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Managed Care Organizations
Nurses
Patients
Physician Assistants
Physicians
Public Health Departments
Respiratory Care Practitioners

GUIDELINE OBJECTIVE(S)

To assist development of national policies to improve the diagnosis and management of smear-negative pulmonary and extrapulmonary tuberculosis

TARGET POPULATION

Adults and adolescents with smear-negative pulmonary and extrapulmonary tuberculosis and human immunodeficiency virus (HIV) infection in HIV-prevalent and resource-constrained settings

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment/Diagnosis

1. Sputum smear examination for acid-fast bacilli (AFB)
2. Laboratory human immunodeficiency virus (HIV) testing
3. Physical examination
4. *Mycobacterium tuberculosis* culture
5. Chest radiograph
6. Lymph node needle aspiration
7. Aspiration of pleural effusion fluid
8. Malaria blood film
9. Cardiac ultrasound
10. Electrocardiogram
11. Lumbar puncture
12. Differential white blood cell count and protein determination
13. Cryptococcal antigen/stain

Treatment/Management

1. Antibiotics
2. Adjuvant corticosteroids
3. Tuberculosis treatment
4. Recording and reporting of cases

MAJOR OUTCOMES CONSIDERED

- Adverse effects of treatment
- Sputum conversion rate
- Patient satisfaction
- Mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Level of Evidence Available for the Recommendations

I. At least one randomized controlled trial with clinical, laboratory or programmatic endpoints
II. At least one high-quality study or several adequate studies with clinical, laboratory or programmatic endpoints
III. Observational cohort data, one or more case-controlled or analytical studies adequately conducted
IV. Expert opinion based on evaluation of other evidence

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Process of Formulation

In September 2005, the World Health Organization (WHO) convened an expert group to review currently recommended approaches to the diagnosis of smear-negative tuberculosis in human immunodeficiency virus (HIV)-prevalent settings and to propose revisions to existing WHO guidelines. The Expert Group has reviewed existing evidence in each of the relevant areas and made recommendations and has revised the existingÂ diagnostic algorithms.

Strength of the Recommendations

The recommendations contained in these guidelines are based on evidence from randomized clinical trials, high-quality scientific studies, observational cohort data and, where sufficient evidence is not available, on expert opinion (see "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields). When appropriate, the level of evidence used to formulate the recommendations is included in the text of the document and shown in the "Rating Scheme for the Strength of the Evidence" field.Â The strength of each recommendation is stated when appropriate, along with the level of evidence, to provide a general indication of the extent to which regional and country programmes should consider implementing the recommendations.

For example, a recommendation marked as A II is a recommendation that should be followed and is based on evidence from at least one high-quality study or several adequate studies with clinical, laboratory or programmatic endpoints. Those recommendations which are based on well established clinical practice are presented as such, without any indication of the level of evidence. For example, the recommendation that calls for an increased level of clinical awareness and competence in managing extrapulmonary tuberculosis at first-level health facilities is not linked with a particular level of evidence. The recommendations do not explicitly consider cost-effectiveness, although the realities of burden of disease, human resources, health system infrastructure and socioeconomic issues need to be taken into account when adapting these recommendations to regional and country programmes.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of the Recommendations

A. Recommended - should be followed

B. Consider - applicable in most situations
C. Optional

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The recommendations and revised diagnostic algorithms were posted on the World Health Organization (WHO) Stop Tuberculosis (TB) Department's web site for an open consultation. Feedback was obtained from national programme managers, researchers, clinicians and other health workers throughout the world, and from all the leading international organizations working on TB. The Expert Group subsequently revised the recommendations and algorithms in the light of the feedback from the global consultation and from presentations at various international scientific meetings.

The Strategic and Technical Advisory Group for Tuberculosis (STAG-TB) and the Strategic and Advisory Committee for Human Immunodeficiency Virus (STAC-HIV), the two independent bodies that advise WHO on TB and HIV respectively, endorsed the recommendations.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The rating schemes for the levels of evidence (I – IV)Â and the strength of the recommendationsÂ (A-C) are defined at the end of the "Major Recommendations" field.

Improving the Diagnosis and Treatment of Smear-Negative Tuberculosis

Revised Case Definitions

The following are suggested case definitions for use in human immunodeficiency virus (HIV)-prevalent settings:

Smear-Positive Pulmonary Tuberculosis

- One sputum smear examination positive for acid-fast bacilli (AFB) **and**
- Laboratory confirmation of HIV infection **or**
- Strong clinical evidence of HIV infection*

Smear-Negative Pulmonary Tuberculosis

- At least two sputum specimens negative for AFB **and**
- Radiographical abnormalities consistent with active tuberculosis **and**
- Laboratory confirmation of HIV infection **or**
- Strong clinical evidence of HIV infection*Â **and**
- Decision by a clinician to treat with a full course of antituberculosis chemotherapy

OR

- A patient with AFB smear-negative sputum which is culture-positive for *Mycobacterium tuberculosis*

Extrapulmonary Tuberculosis

- One specimen from an extrapulmonary site culture-positive for *Mycobacterium tuberculosis* or smear-positive for AFB

OR

- Histological or strong clinical evidence consistent with active extrapulmonary tuberculosis **and**
- Laboratory confirmation of HIV infection **or**
- Strong clinical evidence of HIV infection* **and**
- A decision by a clinician to treat with a full course of antituberculosis chemotherapy

Strength of recommendation: A

*Depending on clinical assessment and national and/or local policy, a person of unknown HIV status may be classified as HIV-positive for the purposes of diagnosis and management.

Antibiotics Trial

- The primary role of antibiotics should not be as a diagnostic aid; they should be used to treat concomitant bacterial infection in people living with HIV/acquired immune deficiency syndrome (AIDS) with cough or serious illness **(Strength: A–IV)**.
- Antibiotic treatment is appropriate for HIV-infected patients with cough, because bacterial infections are common both with and without tuberculosis **(Strength: A–II)**.
- Seriously ill patients with symptoms suggestive of tuberculosis should be treated empirically with broad-spectrum antibiotics because the benefits outweigh the risks **(Strength: A–II)**.
- When indicated, one course of broad-spectrum antibiotics, including coverage for typical and atypical causes of community acquired pneumonia, should be used to reduce the time delay for tuberculosis diagnosis **(Strength: A–IV)**. In such circumstances, fluoroquinolones should be avoided, as they may cause undue delay in the diagnosis of tuberculosis **(Strength: A–II)**.
- More research about the effectiveness and use of an antibiotic trial in the diagnostic algorithm and the choice of antibiotics, particularly for people living with HIV is needed **(Strength: A)**.

Chest Radiograph

- Chest X-ray presentations of tuberculosis in HIV patients are now well characterized and should no longer be considered "atypical" for tuberculosis in HIV-prevalent settings **(Strength: A–IV)**.
- Chest X-rays play a significant role in shortening delays in diagnosis and should be performed early in the course of investigation of a tuberculosis suspect **(Strength: A–II)**.
- Sound clinical judgement is needed to put a seriously ill patient with negative sputum smear results on antituberculosis treatment using only suggestive radiographical findings. In such circumstances, the clinical response of the patient has to be monitored and tuberculosis diagnosis should be confirmed at least by clinical response to antituberculosis treatment and preferably by culture **(Strength: B–II)**.
- The limitations that exist on the wider use of chest X-rays, such as nonavailability at peripheral health facilities and the difficulty of interpreting results, even by trained physicians, need to be addressed, including through training **(Strength: A)**.
- Research is needed to identify innovative ways to enhance the ability of clinicians, including nonphysicians, to interpret chest X-rays accurately, to assess the feasibility and added value of peer reviewing of chest X-rays and to evaluate novel imaging techniques that might replace conventional radiography **(Strength: A)**.

Sputum Culture

- Careful feasibility studies are needed, particularly for liquid culture systems that are more sensitive and rapid than solid culture, and have the potential for expanded use, including in HIV-prevalent and resource-limited settings **(Strength: A–II)**.
- In patients with negative sputum smears, sputum culture should be encouraged as part of the diagnostic procedure for people living with HIV who are being evaluated for AFB smear-negative tuberculosis, since it will improve the quality of care and assist the confirmation of the diagnosis **(Strength: A–I)**.
- Existing capacity for the use of conventional culture systems in countries should be explored, encouraged and strengthened. Decentralization of sputum culture services with an efficient quality assurance system is essential. Establishment of an effective transport system for sputum is also essential **(Strength: A)**.

Immune Reconstitution Inflammatory Syndrome (IRIS) and Tuberculosis Diagnosis

- Tuberculosis should be diagnosed and treated before initiation of antiretroviral treatment and whenever there is clinical suspicion of immune reconstitution inflammatory syndrome (IRIS) **(Strength: A–IV)**
- IRIS is not a reason to switch patients on to second-line antiretroviral treatment, although adjustment to the treatment regimen may be needed to ensure compatibility with antituberculosis treatment **(Strength: A–IV)**.

- Health care workers should be aware of paradoxical worsening of tuberculosis on starting antiretroviral treatment and both antiretroviral and antituberculosis treatments should be continued **(Strength: A–IV)**.

Diagnosis of Extrapulmonary Tuberculosis

- There should be an increased level of clinical awareness and competence in managing extrapulmonary tuberculosis at first-level health facilities, including earlier referral of patients when appropriate **(Strength: A)**.
- In peripheral health facilities in HIV-prevalent settings, clinicians should initiate empirical tuberculosis treatment early in patients with serious illness thought to be due to extrapulmonary tuberculosis. Every effort should then be made to confirm the diagnosis of tuberculosis, including monitoring the clinical response of the patient, to ensure that the patient's illness is being managed appropriately. If additional diagnostic tests are unavailable, and if referral to a higher level facility for confirmation of the diagnosis is not possible, antituberculosis treatment should be continued and completed **(Strength: B–IV)**.
- Empirical trials of treatment with incomplete regimens of antituberculosis drugs should not be performed **(Strength: A–I)**.
- If a patient is treated with empirical antituberculosis drugs, treatment should be with standardized, first-line regimens, which should be used for the entire duration of tuberculosis treatment. Empirical treatment should only be stopped if there is bacteriological, histological or strong clinical evidence of an alternative diagnosis **(Strength: A)**.

Recording and Reporting

- The 2003 recommendation that cases without smear results should be reported as smear-negative pulmonary cases should be revised **(Strength: A)**.
- The revised standard tuberculosis recording and reporting formats should be used to generate sound case-notification and treatment outcome data for smear-negative pulmonary and extrapulmonary cases. This should inform policy and programme performance both nationally and globally **(Strength: A)**.

Simplified and Standardized Clinical Management Guidelines for Extrapulmonary Tuberculosis Diagnosis and Management

Diagnosis and Management

The indications for suspected extrapulmonary tuberculosis and the key signs to look for inÂ the commonest forms of the disease are summarized in Figure 4 in the original guidelineÂ document. The table below summarizes the essential investigations required for diagnosis and key steps for immediate management of suspected extrapulmonary tuberculosis cases. For a patient with suspected extrapulmonary tuberculosis who is started on antituberculosis treatment without bacteriological or histological confirmation, the clinical response to treatmentÂ should be assessed after one month. If there is no improvement, a clinical reassessment should be performed and an alternative diagnosis sought.

HIV testing should be offered to all patients suspected of extrapulmonary tuberculosis. This is because HIV-related extrapulmonary tuberculosis is an indication for early commencement of antiretroviral treatment (clinical stage 4 of HIV disease). For HIV-related extrapulmonary tuberculosis, the following interventions should be carried out:

- Refer for HIV care or start antiretroviral treatment according to national guidelines
- Start co-trimoxazole preventive therapy
- Remain vigilant for clinical deterioration of extrapulmonary tuberculosis after the start of antiretroviral treatment (IRIS) and take appropriate measures

Tuberculous Lymphadenitis

Tuberculous lymphadenitis should be suspected in any patient with enlarged lymph nodes that are firm, asymmetrical, more than 2 cm in diameter, or where a node has become fluctuant or developed a fistula over several months. It most commonly affects the nodes in the neck (cervical region) and is difficult to distinguish clinically from other causes of enlarged nodes, such as reactive and/or HIV-related lymphadenopathy, malignancies and other lymph node infections, which are also common. Therefore, needle aspiration using recommended techniques (see box "Guidelines for lymph node aspiration" in the original guideline document) should be carried out at the first outpatient visit for all patients.

Needle aspiration with cytology and tuberculosis microscopy of aspirated material has a high diagnostic yield, with confirmation of over 85% of patients with tuberculous lymphadenitis in some but not all reports, suggesting that the technique may be important. If a fistula has formed, then microscopy of discharging pus is likely to show AFB. Cytology, if available, can identify most other important causes of enlarged lymph nodes, including malignancies and other infections. Follow-up to receive the results should be within seven days. If the aspirate does not yield a diagnosis, then excision biopsy for gross examination, Ziehl-Neelsen microscopy, mycobacterial culture and, if available, histological examination can be considered.

However, antituberculosis treatment should be started immediately if:

- The patient is HIV-infected and has clinical features of disseminated tuberculosis (such as marked weight loss, rapid clinical deterioration or multiple sites of suspected tuberculosis)

  or

- Tuberculous lymphadenitis is considered the most likely clinical diagnosis, but logistical or economic barriers are likely to delay excision biopsy for two weeks or longer

Pleural Effusion

Tuberculosis is the likely cause of unilateral pleural effusion in countries with a high tuberculosis burden. It was the diagnosis reached in 95% of patients in two recent case-series from Uganda and Zimbabwe. Pleural effusion is the most common form of HIV-related extrapulmonary tuberculosis, with high mortality (over 20%) in the first two months ofÂ tuberculosis treatment. The following key steps should be undertaken:

- The management of tuberculous pleural effusion should aim at starting tuberculosis treatment and identifying underlying HIV infection without delay. Pleural biopsy has a high diagnostic yield, but itÂ is **not** recommended because it is unnecessarily invasive and has the potential to introduce diagnostic delay.
- Suspected pleural effusion should be confirmed by chest radiography and immediate aspiration of fluid whenever possible (see the table below), placing aliquots of the aspirate into one plain and two anticoagulated tubes.
- Treatment with broad-spectrum antibiotics is not required before tuberculosis treatment in patients with unilateral effusions if the pleural fluid is clear and clots on standing, unless there is clinical concern about bacterial pneumonia.
- Patients with unusual findings, such as bilateral effusions, cloudy or bloody aspirates should undergo the additional investigations detailed in the table below. If visible clots form in the aspirate within a few minutes of its being placed into a plain tube (no anticoagulant), then this confirms the high protein content of the fluid, which indicates tuberculosis. No further investigations are needed if the aspirate is clear and straw-coloured and there are no other features suggestive of a diagnosis other than tuberculosis.
- Failure of the aspirate to clot does not exclude tuberculosis, and such patients can still be started on antituberculosis treatment immediately if there are no other unusual findings (seeÂ the table below, but laboratory analysis of fluid is needed to determine the protein content (expect = 30 g/L in patients with a tuberculous effusion, but it can be lower in very wasted patients) and differential cell count (expect = 50% lymphocytes in a tuberculous effusion). The aim should be to start tuberculosis treatment within seven days unless another diagnosis has been made.
- If thoracentesis is not available, antituberculosis treatment should be started immediately, particularly if the patient is HIV-infected, unless there are clinical or radiological features suggestive of a diagnosis other than tuberculosis.

Other Forms of Extrapulmonary Tuberculosis

Most patients with other forms of extrapulmonary tuberculosis present in a sufficiently characteristic way to allow tuberculosis treatment to be started without attempting to confirm the disease bacteriologically or histologically. Although extrapulmonary tuberculosis can be confirmed in the majority of patients through invasive biopsy and/or multiple cultures, these investigations are not routinely recommended, as they are expensive and may result in lengthy diagnostic delays that can reduce the chances of a good treatment response.

Taking specimens for culture increases the chances that tuberculosis will be confirmed, butÂ treatment should not generally be delayed until culture results are available. Instead, tuberculosis treatment should be started promptly, if indicated after the essential investigations and assessments shown in the table

below. The attending health care worker should carefully consider the need for additional investigations and treatment (such as antibiotics) if a diagnosis other than tuberculosis is suspected. However, it is not necessary to give broad-spectrum antibiotics routinely before considering tuberculosis treatment.

Tuberculosis treatment should be started as soon as other common conditions that can cause a similar clinical picture have been excluded (see the table below for essential investigations) in patients presenting with the following conditions:

- Pericardial effusion: tuberculosis is the cause of about 90% of HIV-related pericardial effusion, but a lower percentage (50% to 70%) of pericardial effusions in HIV-negative individuals
- Meningitis with features of the cerebrospinal fluid suggestive of tuberculosis (see the table below)
- Suspected disseminated tuberculosis in febrile patients presenting with HIV wasting syndrome. High rates of undiagnosed disseminated tuberculosis have been consistently identified in febrile, HIV-positive inpatients and in postmortem series from several countries.

Patients with clinical features or investigation results that suggest a diagnosis other than extrapulmonary tuberculosis (listed in the table below) need more extensive investigation before tuberculosis treatment is considered, but with the aim of keeping diagnostic delays to a minimum.

Adjuvant Corticosteroids

Corticosteroids started at the time of tuberculosis diagnosis and given for the first two months of treatment significantly improve survival from tuberculous meningitis in HIV-negative patients, and theyÂ are now recommended for such patients. For other forms ofÂ extrapulmonary tuberculosis and for HIV-related tuberculous meningitis, the effects of steroids are still uncertain. The results of small trials on tuberculous pericarditis are promising. There appears to be no benefit in adding steroids to the treatment of tuberculous pleural effusion, with some suggestion of possible harm to HIV-positive patients. Recommendations may change when the results of larger randomized clinical trials become available within the next few years.

Table. Diagnosis and Immediate Management of Suspected Extrapulmonary Tuberculosis

Lymph Node Tuberculosis (Peripheral)	Pleural Effusion	Disseminated Tuberculosis	
Essential investigations • HIV test (rapid if possible) • Sputum smears if coughing • Needle aspirate for AFB (18 to 21 gauge)	**Essential investigations** • HIV test (rapid if possible) • CXR • Sputum smears if coughing • Aspirate & inspect fluid[b] • Differential white blood cell count and protein	**Essential investigations** • HIV test (rapid if possible) • CXR • Malaria blood	

Lymph Node Tuberculosis (Peripheral)	Pleural Effusion	Disseminated Tuberculosis
	determination (if possible) of aspirate	film • Sputum smears if coughing • Blood cultures, full blood count and cryptococcal antigen

High suspicion of tuberculosis if:
 	
• 2 cm or more in size
• Asymmetrical/localized
• Painless swelling
• Firm/fluctuant/ fistulated
• Cervical location
• Weight loss, night sweats, fever
	High suspicion of tuberculosis if:
	
	• Unilateral effusion
	• Aspirate of fluid[b] is:
	  • Clear and straw coloured and
	  • Clots on standing in a tube without anticoagulants
	• Weight loss, night sweats, fever
	• Evidence for tuberculosis elsewhere
		High suspicion of tuberculosis if:
		
		• Weight loss, fever and cough
		• Abnormal CXR (which can include miliary pattern)
		• Large spleen/liver
		• Night sweats
		• Anaemia

Findings that suggest a non-tuberculosis diagnosis
 	
• KS[a] in skin or mouth (probable KS nodes)
• Symmetrical (probable lymphoma or HIV lymphadenopathy)
• Tender, inflamed, purulent (bacterial or fungal)
• Site other than cervical
	Findings that suggest a non-tuberculosis diagnosis
	
	• Bilateral effusion (possible heart failure or pneumonia)
	• Clinical KS[a]/other malignancy
	• Aspirate of fluid is:
	  • Cloudy/pus (probable empyema)
	  • Fails to clot (does not exclude tuberculosis, but send fluid for protein and
		Findings that suggest a non-tuberculosis diagnosis
		
		<u>if HIV+ consider Salmonella, pneumococcus, malaria, Cryptococcus</u>
		
		• Rigors
		• Very breathless

Lymph Node Tuberculosis (Peripheral)	Pleural Effusion	Disseminated Tuberculosis
	differential cell count, and consider heart failure)	(respiratory rate >30/min) • Severe diarrhoea • Blood in stool • Positive cryptococcal antigen, malaria smear or likely pathogen isolated from blood culture

Immediate management
 	
• Aspirate for cytology and AFB microscopy
• Excision biopsy if aspirate non-diagnostic unless:
  • HIV+ with possible disseminated tuberculosis (e.g., rapid clinical deterioration)
  • Tuberculosis considered the most likely clinical diagnosis, and biopsy not available within 2 weeks
	Immediate management
	
	Features of tuberculosis only
	
	• Start tuberculosis treatment
	
	Â *Features of non-tuberculosis diagnosis*
	
	• Send aspirate for differential cell count, protein and, if available, cytology: ≥50% lymphocytes and protein >30 g/L suggests tuberculosis
	• Treat for tuberculosis if the only unusual feature is failure of aspirate to clot, or no other diagnosis by 7 days
		Immediate management
		
		Features of tuberculosis only
		
		• Start tuberculosis treatment (add antibiotics if critically ill)
		
		Features of non-tuberculosis Diagnosis
		
		• Investigate other causes
		• Start both tuberculosis treatment and antibiotics if critically ill

[a] KS-Kaposi's sarcoma

[b]The aspirate should be put in a plain tube (with no anticoagulant) in order to observe its appearance and clotting. A second aliquot should be placed into an anticoagulated tube, so that a differential white blood cell count and protein determination can be requested if there are any findings to suggest a non-tuberculosis diagnosis.

Definitions:

Strength of the Recommendations

A. Recommended – should be followed
B. Consider – applicable in most situations
C. Optional

Levels of Evidence

I. At least one randomized controlled trial with clinical, laboratory or programmatic endpoints
II. At least one high-quality study or several adequate studies with clinical, laboratory or programmatic endpoints
III. Observational cohort data, one or more case-controlled or analytical studies adequately conducted
IV. Expert opinion based on evaluation of other evidence

CLINICAL ALGORITHM(S)

Clinical algorithms are provided for:

- Diagnosis of tuberculosis in ambulatory human immunodeficiency virus (HIV)-positive patient
- Diagnosis of tuberculosis in seriously ill patient in HIV-positive patient
- Diagnosis of tuberculosis in HIV-negative patients

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is specifically stated for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of adults and adolescents with smear-negative pulmonary and extrapulmonary tuberculosis in human immunodeficiency virus (HIV)-prevalent settings

POTENTIAL HARMS

Adverse events associated with treatment are common during treatment ofÂ human immunodeficiency virus (HIV)-associated tuberculosis.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

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IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Evaluation

In the absence of complete evidence, the recommendations were built on consensus and iterative global expert opinion. It is believed that they will provide a reasonable response to the catastrophe posed by the dual tuberculosis and human immunodeficiency virus (HIV) epidemics. These recommendations should therefore be implemented in HIV-prevalent settings in order to improve and expedite the diagnosis of tuberculosis among people living with HIV. The implementation of the recommendations requires a reasonably efficient health system, including quality assurance for laboratories and effective supply management and training for programme staff. Moreover, depending on country-specific-factors, it may require revision of national guidelines, logistical and technical arrangements including human resources, training and infrastructure development. While the recommendations are being implemented, it is essential to build up the evidence base required to assess their effectiveness and feasibility. Careful evaluations by national authorities, research groups and interested parties are needed to assess the likely benefits and responsiveness of the recommendations for the dual tuberculosis and HIV epidemics. The findings of these evaluations will inform policy change designed to improve programme performance both globally and nationally. A protocol for operational evaluation of the revised recommendations and algorithms for improving the diagnosis of tuberculosis in HIV-prevalent settings are provided as an annex to the original guideline document.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

World Health Organization (WHO). Improving the diagnosis and treatment of smear-negative pulmonary and extrapulmonary tuberculosis among adults and adolescents. Recommendations for HIV-prevalent and resource-constrained settings. Geneva: Switzerland: World Health Organization (WHO); 2007. 36 p. [33 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007

GUIDELINE DEVELOPER(S)

World Health Organization - International Agency

SOURCE(S) OF FUNDING

World Health Organization

GUIDELINE COMMITTEE

World Health Organization (WHO) Expert Group on Smear-Negative TB

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the World Health Organization Web site. Also available in FrenchÂ and Spanish.

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Getahun H et al. Diagnosis of smear-negative pulmonary tuberculosis in people with HIV infection or AIDS in resource-constrained settings: informing urgent policy changes. Lancet 2007;369:2042-49.

PATIENT RESOURCES

None available

NGC STATUS

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Date Modified: 3/1/2010